Illinois Department of Public Health
Lysosomal Storage Disease (LSD) Ad Hoc Subcommittee
Conference Call Minutes - May 9, 2011

Subcommittee Members Attending
Dr. Barbara Burton – Children's Memorial Hospital
Dr. Joel Charrow – Children's Memorial Hospital
Dr. Kathy Grange – Washington University St. Louis Children's Hospital
Dr. George Hoganson – University of Illinois
Dr. Darrel Waggoner – University of Chicago
Tess Rhodes – University of Illinois, Division of Specialized Care for Children
Dr. Michael Schneider – Southern Illinois School of Medicine

Guests
Bob Evanosky – Parent
Representatives - Advanced Liquid Logic, Inc.

IDPH Staff

Dr. George Dizikes	Claudia Nash
Dr. David Culp	Heather Shryock
Tom Schafer	Barbara DeLuka
Tom Johnson	Margie Nelson
Dr. Mike Petros	
Dr. Rong Shao	

The meeting was convened by the Chair, Dr. Barbara Burton, via conference call at 11 AM.

Discussion
Dr. Burton reviewed data distributed by Newborn Screening Program staff and Dr. George Dizikes in advance of the meeting. A total of 7557 infants were screened in the LSD pilot through April 16, 2011. A total of 11 positive screening tests for Fabry disease were reported. Of these there are 4 confirmed cases of Fabry disease and 2 others that are presumed to be affected (low enzyme activity, DNA pending). Another case was found to have slightly low enzyme activity and also has mutation testing pending. Four cases are confirmed normal. There was general agreement among committee members that the Fabry assay is working very well with few false positives. One committee member expressed surprise that the incidence of Fabry disease appears to be so high. However, it was noted that this is in keeping with the findings of pilot studies in Italy and Taiwan.

A total of two positive results have been reported for Pompe disease. Both infants were found to be normal on confirmatory testing. The committee was in agreement that the Pompe assay appears to be working very well.

A total of 19 positive results have been reported for Gaucher disease. 11 of the 19 have been in infants in NICU's, 8 of whom weighed less than 1000 grams. There have been 3 positive diagnoses of Gaucher disease, two in full term non-NICU infants and one in a small premature infant who had an initial positive screen followed by a normal screen (after transfusion). The confirmatory enzyme testing in the latter infant was performed at 3 months of age. There was some discussion of how positive test results in NICU infants should be approached. The impact of transfusion has not yet been determined. Up until now, the approach has been determined on a case by case basis with some cases closed following a normal repeat newborn screen. No definite decision was made on the appropriate approach.

Dr. Dizikes reported to the committee on the experience in the lab thus far in running the assays. He reported that there have been problems with a large number of failed runs, primarily related to poor performance of the cartridges on the QC samples, causing the run to be aborted. He also stated that the vendor, Advance Liquid Logic, Inc. (ALL), has not met the timeline laid out in the contract for delivering the Krabbe and Niemann-Pick assays or for delivering the 48 sample cartridges and additional equipment necessary to expand to statewide screening. Dr. Dizikes agreed that the Fabry and Pompe assays are performing well and indicated that the primary problem is with the Gaucher assay. He stated that there is wide variability in the results from run to run. Representatives from ALL on the call indicated that they are developing a solution to the problem of inconsistency in the Gaucher assay and believe that the problem can be solved. They also stated that the 48 sample cartridges and several additional machines would be in the IDPH lab the week of May 16.

Some discussion ensued with regard to the Gaucher assay and whether the Department is engaged in research in the development of this assay. The committee acknowledged that the purpose of a pilot phase in introducing a new test is to work out the glitches and fine tune the assay in the real world setting. Some individuals on the call felt that the problems ongoing with the ALL Gaucher assay went beyond this such that the current efforts would be classified as research and development. Others disagreed. Dr. Waggoner questioned whether the state and individual hospitals might have legal liability if cases of Gaucher disease were missed due to an inaccurate assay. Dr. Dizikes indicated that he was considering notifying the two hospitals in the pilot that the lab would be no longer screening for Gaucher disease. He had not made a definite decision and stated that he would notify the committee when this decision is made. Dr. Charrow indicated that he felt we were better off continuing to screen since it is clear that the current assay detects some cases of Gaucher disease, even though there is the potential for missed cases with a high degree of assay variability.

The lab was asked if they anticipate moving to statewide screening on the previously announced date of June 1, 2011. Dr. Dizikes stated that this would not be possible and ALL concurred. Neither the lab director nor ALL wanted to predict when this would be possible.

Tom Johnson announced that IDPH had decided that they would not renew their contract with ALL which expires at the end of June, 2011. He indicated that the Department wanted to explore the option of doing the LSD assays by MS/MS. There was considerable discussion at this point. Representatives from ALL indicated that they were confident that the problems with reproducibility of the assays and failed runs could be overcome and that the high throughput system would shortly be in place. They stated that they were certain that this would put IDPH in position to do statewide screening much sooner than would be possible with MS/MS. Bob Evanosky pointed out that the intent of the legislation signed into law in November, 2007, was that testing for the 5 LSD's would be done by MS/MS since that was the only technology available at that time. He also pointed out that the Department had chosen to go with ALL, with the full knowledge that their system had not been tested in the newborn screening setting and that the Krabbe and Niemann-Pick assays had not been developed when the contract was signed. Dr. Culp stated that this prolonged pilot screening with multiple reruns was taxing the resources of the newborn screening lab. Everyone on the call agreed that the goal is to implement statewide screening for the 5 LSD's as soon as possible, but that a reliable test must be in place before this can occur. There was concern expressed that a switch to MS/MS would delay the implementation of statewide screening and could result in higher costs. In addition, it was pointed out that MS/MS screening for the 5 diseases in a multiplex system has not been done on a newborn screening population – therefore there is no guarantee that problems will not be encountered in that system, just as they have been with the digital microfluidic system.

Dr. Grange indicated that the plan in Missouri is to begin pilot screening for the LSD's in January 2012. 5 LSD's will initially be included – Fabry, Pompe, Gaucher, MPSI and MPS II. Only abnormal results would be reported during that time. Full screening and reporting would take place as of summer, 2012. At this time, the plan in Missouri is to use the ALL system.

It was decided that IDPH would keep the committee informed of their decisions with regard to the Gaucher assay and the ALL system. Another subcommittee meeting will be scheduled in approximately 2 months.

Minutes prepared by Dr. Barbara Burton
May 10, 2011